

## REMARKS

The Office Action at page 5 asserts US patent 6,444,448 to **Wheatcroft**.

- 1) **Wheatcroft's patent** deals with a glucan-mannan complex, while the present invention claims exclusively  $\beta$ -D-glucan preparation. Thus, the two cases (the reference and the claimed invention) deal with *different compounds* (see also comment 5).
- 2) In **Wheatcroft's patent**, the polysaccharide complex is prepared by autolysis, whereas the claimed invention uses alkaline extraction (see also comment 3).
- 3) In **Wheatcroft's patent**, no deproteination of the resulting compound is described, which may lead to contamination of the final product with potentially toxic and certainly immunogenic proteins that may elicit adverse reaction when used in pharmaceutical/cosmetic/food preparations. The product stemming from the procedure described by the claimed invention avoids such possibility by eliminating proteins at an alkaline extraction step and subsequent removal of water-soluble components (including denaturated proteins and peptide fragments). the claimed invention quotes nitrogen content in a resulting product, while **Wheatcroft** does not provide any proof of purity, on the contrary, Table 1 indicates that "Autolytic Glucan" contains 27 % protein.
- 4) **Wheatcroft's patent** uses yeast model, specifically brewer's yeast (*Sacharomyces cerevisiae*), while the claimed invention uses edible macroscopic mushroom *Pleurotus ostreatus*. Thus, the two cases (the reference and the claimed invention) deal with *different natural sources*. **Wheatcroft** only mentions *Pleurotus* among other potential sources of  $\beta$ -D-glucan (see also comment 5).
- 5) *Pleurotus ostreatus* is **not** a microorganism and does not belong to yeasts. As not being such, it does not contain mannan in its cell walls and therefore the product isolated and described by the claimed invention is totally chemically **distinct** from that presented in **Wheatcroft's patent**.
- 6) Changes in the properties of polysaccharide (glucan or glucan-mannan) preparations described in Table VIII of **Wheatcroft's patent** as attained by varying the used pH, enzyme application, or different physico-chemical treatments (boiling, milling) can only change the viscosity (extrinsic property), but cannot change chemical nature (monosaccharide composition, chemical bonds, branching (intrinsic properties) of the polysaccharides, and thus the  $\beta$ -D-glucan prepared from *Pleurotus ostreatus* by using the procedure presented by the claimed invention cannot be manufactured from the product rendered by the procedure described in **Wheatcroft's patent** even by a person skilled in the in the art.
- 7) **Wheatcroft's patent** contains many factual imprecisenesses and even errors, e.g. incorrect names of fungi Schizophylla, Fachyma hoelen; quoting  $\beta$ -1,2 and  $\beta$ -1,4 glucans among those that may be present in the yeast preparation, although the former does not exist in nature, while the latter is the plant glucan – cellulose; the results of methylation analysis presumably used to assay linkages in the produced samples has no predictive value since methylation cannot differentiate between mannosyl and glucosyl units and therefore it is not obvious, in which

polysaccharide component which linkages occurred, whereas the glucan isolated by the claimed invention is precisely characterized.

- 8) Patent application Hunter (US2002/0192280) describes use of chemical sterilizers including benzoic acid in preparations distinct from that suggested by the claimed invention (not  $\beta$ -D-glucan hydrogel).

By reason of the foregoing, reconsideration is requested.

/s/

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PTO Reg. No. 32746